

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 30 January 2001 (30.01.01)	
International application No. PCT/AU00/00680	Applicant's or agent's file reference 2306081
International filing date (day/month/year) 16 June 2000 (16.06.00)	Priority date (day/month/year) 18 June 1999 (18.06.99)
Applicant WU, Wen-Yang et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
21 December 2000 (21.12.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer R. E. Stoffel Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY
PCT
INTERNATIONAL PRELIMINARY EXAMINATION REPORT

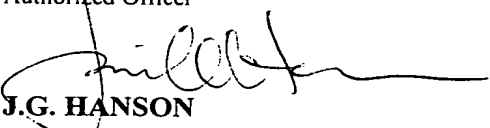
(PCT Article 36 and Rule 70)

REC'D 10 JUL 2001

WIPO PCT

Applicant's or agent's file reference 2306081/ MJC/RR	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/AU00/00680	International Filing Date (<i>day/month/year</i>) 16 June 2000	Priority Date (<i>day/month/year</i>) 18 June 1999
International Patent Classification (IPC) or national classification and IPC Int. Cl.⁷ C07D 401/04, 403/04, 261/08, 237/10, 417/04; A61K 31/80. 31/42, 31/50, 31/4453; A61P 31/12		
Applicant BIOTA SCIENTIFIC MANAGEMENT PTY LTD et al		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of 5 sheets, including this cover sheet. <input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of 11 sheet(s).
3.	This report contains indications relating to the following items: I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 21 December 2000	Date of completion of the report 4 July 2001
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer  J.G. HANSON Telephone No. (02) 6283 2262

I. Basis of the report

1. With regard to the **elements** of the international application:*
- ☐ the international application as originally filed.
- ☒ the description, pages **1, 2, 4-66**, as originally filed,
pages , filed with the demand,
pages **3**, received on **23 March 2001** with the letter of **23 March 2001**
- ☒ the claims, pages **68, 70-77** , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages **67, 69, 79-82, 84, 85** received on **23 March 2001** with the letter of **23 March 2001**
page **78** received on **9 May 2001** with the letter of **9 May 2001**
pages **83** received on **15 May 2001** with the letter of **15 May 2001**
- ☐ the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of
- ☐ the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of
2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:
- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished
4. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.
5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be nonobvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos: **1-16 (part) and 23-31 (part).**

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claim Nos. **1-6 (part) and 23-31 (part).**

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-23, 25, 27-31	YES
	Claims 24, 26	NO
Inventive step (IS)	Claims 1-23, 25, 27-31	YES
	Claims 24, 26	NO
Industrial applicability (IA)	Claims 1-31	YES
	Claims	NO

2. Citations and explanations (Rule 70.7)

- D1 WO 90/01874
(Relevant to claims 1, 2, 3, 5, 6, 8, 10-13, 15, 16 and 21-25).
- D2 Patent Abstract of Japan, JP 8081314 A; See abstract.
(Relevant to claims 1, 2, 3, 5, 8, 10 11, 15, 16, 21, 24 and 25).
- D3 Patent Abstract of Japan, JP 5-320117 A; See abstract.
(Relevant to claims 1, 2, 5, 6, 8, 10, 11, 15, 16, 24 and 25).
- D4 US 4472416
(Relevant of claims 1, 3, 8-13, 15, 16, 23-25).
- D5 EP 290906
(Relevant to claims 1, 3, 8, 10-13, 15, 16, 23-25).
- D6 J. Med. Chem., Vol. 38 (7), 1995 pages 1119-1131; See compound 65, table 2, page 112
(Relevant to claims 24-26
- D7 Indian Journal of Chemistry, Vol. 15 (8), 1977 pages 715-719; See compound 14, table 1 page 717
(Relevant to claims 24-26
- D8 J. Med. Chem., Vol. 39 (1), 1996 pages 237-245; See compounds 10a and 10b, page 239
(Relevant to claims 24-26

Continued in Supplemental Box.

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of VNovelty (N): Inventive Step (IS).

The amended claims are considered in the groupings (a) and (b) below:

- (a) The oxime ethers and their pharmaceutical applications of claim 1-23, 25 and 27-31.
- (b) The oximes and their pharmaceutical applications of claims 24 and 26.

With respect to group (a) claims, the compounds of citations of citation D1 to D3 are now excluded by proviso. The compounds of citations D4 and D5 are excluded because the "alk" link of the claimed compounds appears to exclude the substituted forms of this prior art. Finally, the compounds of citations D6 to D8 are excluded as these claims define oxime ethers instead of the oximes of this prior art.

Accordingly, these claims of group (a) are novel.

Whilst the prior art of citations D6 to D8 does suggest possible pharmaceutical uses for the oximes, the specific nature of these disclosures would not seem to lead a skilled person to verify similar activities in the modified oxime ether forms of these claims.

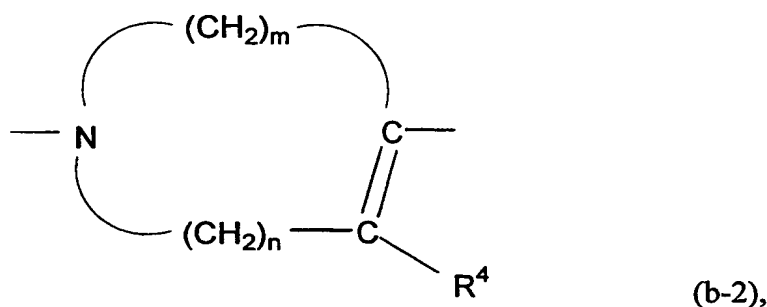
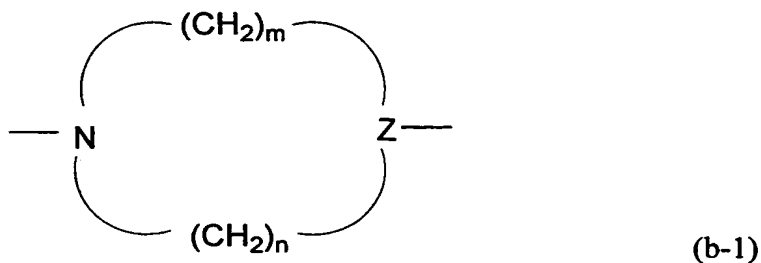
Accordingly, the claims of group (a) also involve an inventive step.

With respect to group (b) claims, claim 24 includes the oximes disclosed in citation D6 to D8. Also, this prior art indicates possible pharmaceutical uses for these oximes.

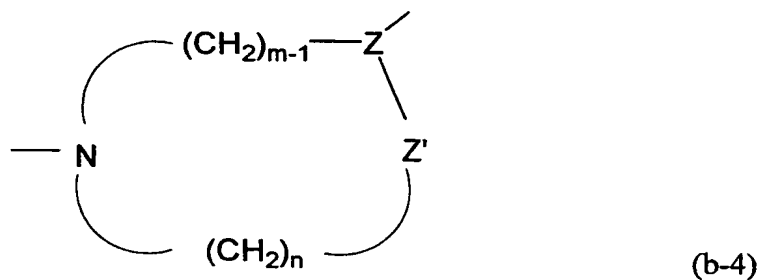
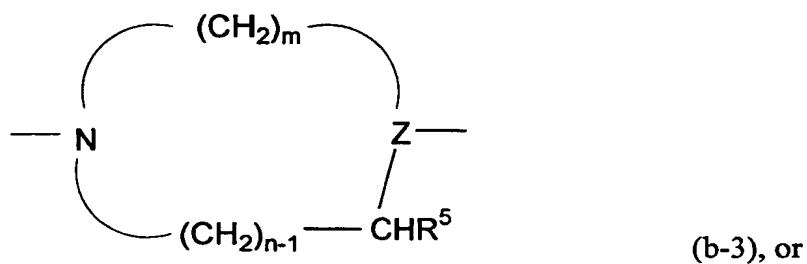
Accordingly, claim 24 and the associated pharmaceutical compositions of claim 26 are not novel and lack an inventive step in light of citations D6 to D8.

- 3 -

A is O, S, NH, N(C₁₋₆alkyl), CH₂O, a bond or a bivalent heterocyclic radical of the formula



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where one or more of the carbon atoms within the radicals (b-1) to (b-4) may be optionally substituted with C₁₋₆alkyl or two carbon atoms in the radicals (b-1) to (b-4) may be bridged with a C₂₋₄alkylene radical, m and n are each

- 67 -

CLAIMS:

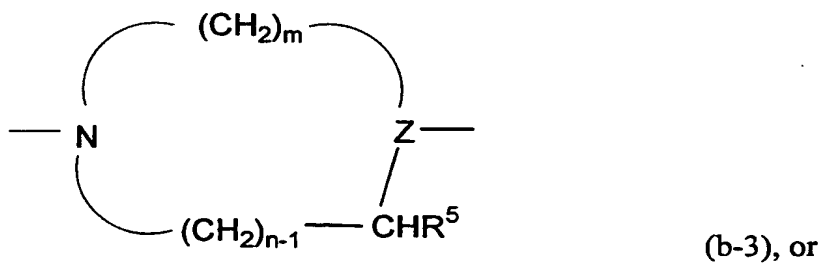
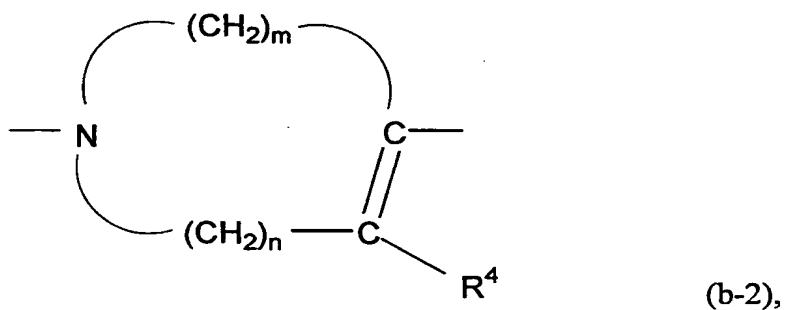
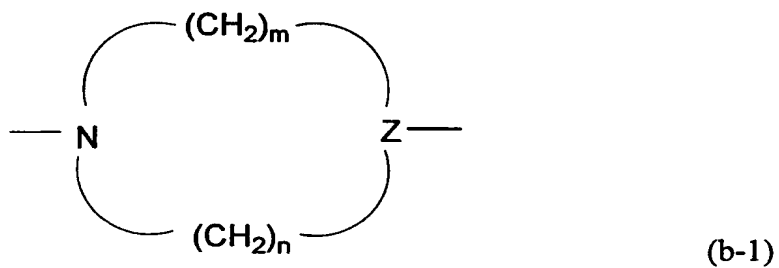
1. A compound of formula I



its salts, and pharmaceutically acceptable derivatives thereof where

- 10 Het is an optionally substituted 5- or 6-membered monocyclic heterocyclic radical or an optionally substituted 9- or 10-membered bicyclic heterocyclic radical;

A is O, S, NH, N(C₁₋₆ alkyl), CH₂O, a bond or a bivalent heterocyclic radical of the formula



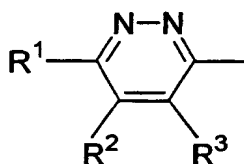
- 69 -

X^1 is C_{1-6} alkyl, C_{3-6} alkenyl, C_{3-6} haloalkenyl, C_{3-6} alkynyl, C_{3-6} haloalkynyl or C_{1-6} alkyl substituted by halo, cyano, nitro, hydroxy, aryl, C_{1-4} alkoxy, C_{2-6} alkoxyalkoxy, acyl or C_{1-4} alkylthio; and

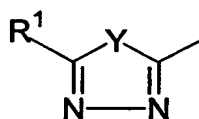
- 5 X^2 is hydrogen, cyano, F, Cl, C_{1-4} alkyl, C_{1-4} haloalkyl or a bivalent radical of formula $-(CH_2)_2-$, $-(CH_2)_3-$, $-CH_2O-$ or $-(CH_2)_2O-$ which forms a 5- or 6-membered ring with a neighbouring carbon atom of Ar.

2. A compound according to claim 1 wherein Het is a radical selected from:

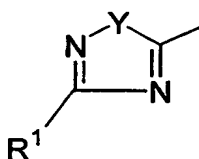
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(a-1)

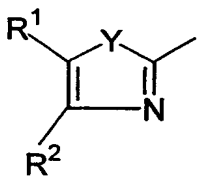


(a-2)

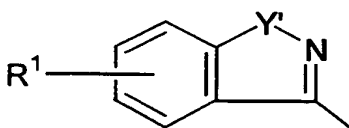


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(a-3)



(a-4)



(a-5)

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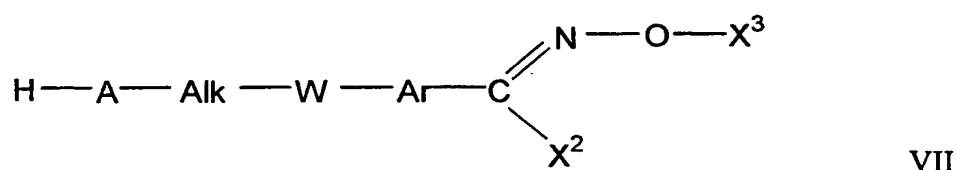
- 78 -

X^2 is hydrogen, cyano, C_{1-4} alkyl, C_{1-4} haloalkyl or X^2 is $-CH_2CH_2-$ or $-CH_2CH_2CH_2-$ forming a 5- or 6-membered ring with a carbon atom on the phenyl ring.

22. A compound of formula I as described in any one of Tables 1 to 8.

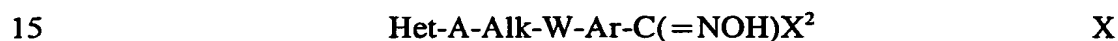
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23. A compound of formula VII:



10 where A, Alk, W, Ar and X^2 are as defined in claim 1, and X^3 is X^1 or an oxime protecting group.

24. A compound of formula IX



where Het, A, Alk, W, Ar and X^2 are as defined in claim 1.

20 25. A composition comprising a compound of formula I according to claim 1 together with a pharmaceutically acceptable carrier.

26. A composition according to claim 24 which is a pharmaceutical composition.

25 27. A composition according to claim 24 further including a known anti-viral or anti-retroviral agent or other pharmaceutical used in the treatment of viral infections.

28. A method for the treatment or prophylaxis of a picornavirus infection in a mammal including the step of administering an effective amount of a compound of formula I as claimed in claim 1.

- 79 -

29. A method of claim 27 wherein the picornaviral infection is caused by one or more serotypes of rhinovirus.

5 30. Use of a compound of formula I in the manufacture of a medicament for the treatment or prophylaxis of picornavirus infection in mammals.

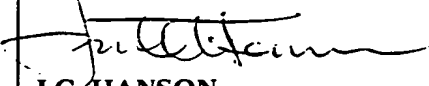
31. Use according to claim 30 wherein the picornavirus infection is one caused by one or more of the serotypes of rhinovirus.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 00/00680

A. CLASSIFICATION OF SUBJECT MATTER		
Int Cl ⁷ : CO7D 401/04, 403/04, 261/08, 237/10, 417/04, A61K31/501, 31/42, 31/50, 31/4453 A61P 31/12		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) STN: FILE CA Chemical Structure Search.		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 90/01874 (Teijin Limited) 8 March 1990 See claim 1	1,2,3,5,6,8,10- 13,15,16,21-25
X	Patent Abstracts of Japan. JP, 8081314 A (Kumiai Chem Ind Co Ltd et al) 26 March 1996 See abstract	1,2,3,5,8,10,1115,16, 21,24,25
X	Patent Abstracts of Japan, C117, page 90 JP 5-320117A (Teijin Ltd) 3 December 1993. See abstract	1,2,5,6,8,10,1115,16, 24,25
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
<p>* Special categories of cited documents:</p> <p>"A" Document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p>		
Date of the actual completion of the international search 1 August 2000		Date of mailing of the international search report - 3 AUG 2000
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200 WODEN ACT 2606 AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No.: (02) 6285 3929		Authorized officer  J.G. HANSON Telephone No.: (02) 6283 2262

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU 00/00680

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4472416 A (Bayer Aktiengesellschaft) 18 September 1984.	1,3,8-13, 15,16,23-25.
X	EP290906 A (Bayer AG) 17 November 1988	1,3,8,10-13, 15,16,23-25.
X	J. Med. Chem Vol 38(7), 1995, pages 1119-1131 Strupczewski et al "3-[[[Aryloxy]alkyl].....(HP873) See compound 65, table 2, page 1122.	24
X	Indian Journal of chemistry Vol 15(8), 1977, pages 715-719 Starling et al. "anti-inflammatory.....propanes". See compound 14, table 1, page 717.	24
X	J. Med. Chem Vol 39(1), 1996, pages 237-245 Malamas et al. "Azole Phenoxy.....5-Lipoxygenase". See compounds 10a and 10b, page 239.	24

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/AU 00/00680

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-16 and 23-31
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
A complete search could not be carried out for economic reasons. The search has therefore been carried out largely on the basis of the specific examples.
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/AU 00/00680

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
WO	9001874	AU	23092/88	EP	433451	WO	9002113
		JP	4500074	ZA	9001158		
JP	8081314	NO	FAMILY	MEMBERS			
JP	5-320117	NO	FAMILY	MEMBERS			
US	4472416	AR	231833	AT	20058	AU	86077/82
		BR	8204776	CA	1185981	CS	228938
		DD	206528	DE	3132335	DK	3646/82
		EG	15752	EP	76370	ES	515031
		GR	76255	HU	190409	IE	53871
		IL	66542	JP	58039670	JP	61046474
		KR	8901547	NZ	201578	PL	237928
		PL	133290	PT	75398	US	4472416
		ZA	8205912				
EP	290906	AU	1585388	BR	8802329	DE	3716023
		DK	2647/88	EP	290906	JP	63297378

END OF ANNEX